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THE

British Medical Journal

THE JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

INCLUDING

AN EPITOME OF CURRENT MEDICAL LITERATURE.

EDITED FOR THE ASSOCIATION BY

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the disease shall run the course of a true septicaemia, with numerous parasites occurring and multiplying in the general circulation, or whether their presence shall be restricted to certain of the internal organs, appears to be mainly the resistance of the particular species. The experiments of Bruce,[3] Laveran and Mesnil,[4] Plimmer and Bradford,[5] and of Mantini,[6] show the widely separated limits of the time required by the trypanosoma of nagana to cause death in the different species investigated. Thus, the very susceptible rat dies in a few days, while the guinea-pig may live for several months. Speaking generally, the more resistant the species or individual, the less likely are we to find the organisms in numbers in the peripheral blood during life. Taking the white rat, again, as an example we find the parasites appearing in the blood three or four days after inoculation; they then increase enormously in numbers until, just before death, they may be almost as numerous as the red blood corpuscles. On the other hand, in the rabbit, which shows a considerably greater power of resistance, death being postponed frequently for a month or six weeks, parasites can only rarely be found, and frequently the most careful search of several films fails to demonstrate a single trypanosoma, the organisms in this case being found in large numbers either in some of the internal organs and the bone marrow, or forming accumulations in the lymphatics of certain regions, such as the eye or the genital organs.

It is thus evident that a fatal attack of trypanosomiasis in an animal does not necessarily postulate the occurrence of the parasites in the peripheral blood, in numbers large enough to permit of microscopical detection.

Again, the chronic nature of the disease in the few recorded cases of trypanosomiasis in man and the immunity which man appears to possess to infection by other varieties of trypanosoma, such as nagana, surra, dourine, *mal de caderas*, etc., would appear to show that man is very resistant to trypanosoma infection.

It is not, then, I think, unreasonable to assume, first, that when trypanosomiasis does occur in man the parasites are more likely to multiply and accumulate in the capillaries or lymphatics of the internal organs than to invade the general circulation in large numbers; and, secondly, that the cases which have been recently reported are in reality exceptional cases, in which the resistance of the individual was comparatively low, and in which the parasites were able to develop and multiply in the blood stream, as they do in the case of a horse, rat, or mouse infected by trypanosoma brucei.

It appears to me, therefore, as at least possible that trypanosomiasis may be a much commoner disease of tropical countries, including India, than is generally supposed, and that its non-recognition may be due, as I have suggested above, partly to the tendency of the parasite to confine itself to the internal organs during the life of its host, and partly to the rapid degeneration and loss of characteristic shape which follow on the death of the organism and render its identification, in sections or smear preparations, a matter of difficulty. This difficulty is further increased by reason of the fact that only by Romanowsky staining can the macronuclei and micro-nuclei be rendered visible, and then only in smear preparations, since it is very hard to produce satisfactory chromatin staining in sections owing to the chemical alterations induced in the tissues by the various processes of hardening and embedding. I have tried to modify these processes in various ways, but so far without success.

With a view, then, to finding out whether some of these severe tropical cachexias, such as the Dum-dum fever, may not be due to trypanosomiasis, I would suggest that, as a routine practice, necropsies of such cases should include the staining of smear preparations from the spleen, lungs, and liver by Romanowsky's method, and a careful search for the degeneration forms of the parasites which I have described.

Increased facilities for the detection of trypanosomiasis during life are much to be desired. Positive results might be obtained by inoculation of a susceptible animal with blood from a suspected case, although this procedure does not appear to have been successful in Dr. Manson's case, and Drs. Annett and Dutton record that the pathogenicity of the trypanosoma in their case was not marked in white rats. Possibly the monkey might prove more susceptible to the trypanosoma of man. Some of the methods of staining thick blood films by dissolving out the haemoglobin, such as those of Laveran and of Ross, may also give an increased chance of success, and in this connexion I may note that the modification of Romanowsky's stain, described by me in the BRITISH MEDICAL JOURNAL,[7] may be utilized for this purpose by mixing a little of the stain with twice its volume of water, pouring the mixture on to the unfixed film, and at the end of three or four minutes gently washing it off, when the film may be dried and mounted. It has also been suggested that larger quantities of blood may be examined by citrating it and employing the centrifuge.

I would further suggest, in conclusion, that the procedure I have indicated might possibly be of service in the investigation of kala-azar and of sleeping sickness, both of which have recently been considered as perhaps due to trypanosomiasis.

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[1] BRITISH MEDICAL JOURNAL, September 20th, 1902. [2] Ibid, March 1st, 1903. [3] *Preliminary Report on the Tsetse Disease or Nagana*, 1895; also Report, 1897. [4] *Extrait du Bulletin de l'Académie de Médecine*, June 10th, 1902. [5] *Quarterly Journal of Microscopical Science*, February, 1902. [6] *Zeitschrift f. Hygiene*, vol. xlii, p. 341, 1903. [7] BRITISH MEDICAL JOURNAL, September 21st, 1902.

THREE CASES OF TRYPANOSOMA IN MAN IN ENTEBBE, UGANDA.

By C. J. BAKER, L.R.C.P., M.R.C.S.,
Medical Officer, Entebbe, Uganda.

CASE I.—A native policeman came to the dispensary at Entebbe on March 12th, 1903, suffering from pain in the head and on finding his temperature was over 102° F. I examined a fresh film of his blood for possible malarial parasites. Though unsuccessful in this direction, I discovered an elongated, actively motile body which, on closer inspection, I made out to be a trypanosoma. I called in Dr. Mole, P.M.O. Uganda, and Dr. Castellani, of the Sleeping Sickness Commission, who both happened to be close at hand, and they were able to give their valuable confirmation to my diagnosis. I afterwards found about a dozen of these parasites in the same slide. On admission, the patient, a native of the Usoga district, stated that he had never been outside the Uganda Protectorate, and had lived for the past 12 months in Entebbe, except when he had made three journeys to Masindi (Unyoro district). He had never to his knowledge been bitten by any cattle-biting fly, but had been badly bitten by leeches about a year previously. He had never had a similar attack before, and had been quite well up to two days before admission, when he began to complain of general headache. His temperature was 102.6°, his pulse-rate 100 per minute, and respirations were normal, his organs on examination appeared perfectly healthy, the spleen not being enlarged, and there was no oedema of the skin. After admission his temperature on the second day reached 104°, after which it begun to fall, reaching normal on the fifth day, though he underwent no treatment. At the same time the parasites gradually diminished in number and apparently disappeared from the blood on the same day as the temperature reached normal, and subsequent daily examination of his blood produced only negative results.

CASE II.—Kumour Saba, a native policeman, came to the dispensary on March 28th, 1903, suffering from headache and having a temperature of 101.8°, I examined his blood and found a single trypanosoma, which was also seen by Dr. Nabarro. On admission his temperature was 101.8°, his pulse was 92, and there was the same slight general headache as in the first case. He stated he was one of the Lendu tribe, and had migrated from the west side of the Albert Nyanza about 1895, since when he had been in the Buddu district of Uganda up till 10 months ago, after which he has always resided at Entebbe. He could give no history of having been bitten by any biting fly, and had had no previous similar attack. He was quite well up to the day before admission. On examination his spleen and other organs appeared to be normal, and there was no oedema of the skin. Though I have carefully examined several films of his blood, I have not found a single trypanosoma other than the one mentioned above. His temperature dropped to 99° on the second day, and became subnormal on the fifth day after admission, there being a slight rise on the third and fourth days. All headache left him on the second day.

CASE III.—Jardien Murjan, a prisoner, was admitted to hospital on March 31st. On admission his temperature was 101.8°, pulse 110 per minute, respirations normal, and he complained of severe headache. On examination of his blood I found several trypanosomes. His spleen was slightly enlarged but not tender, and he had slight oedema of the skin over the abdomen extending upwards over the lower ribs. He could give no history of a previous similar attack, and

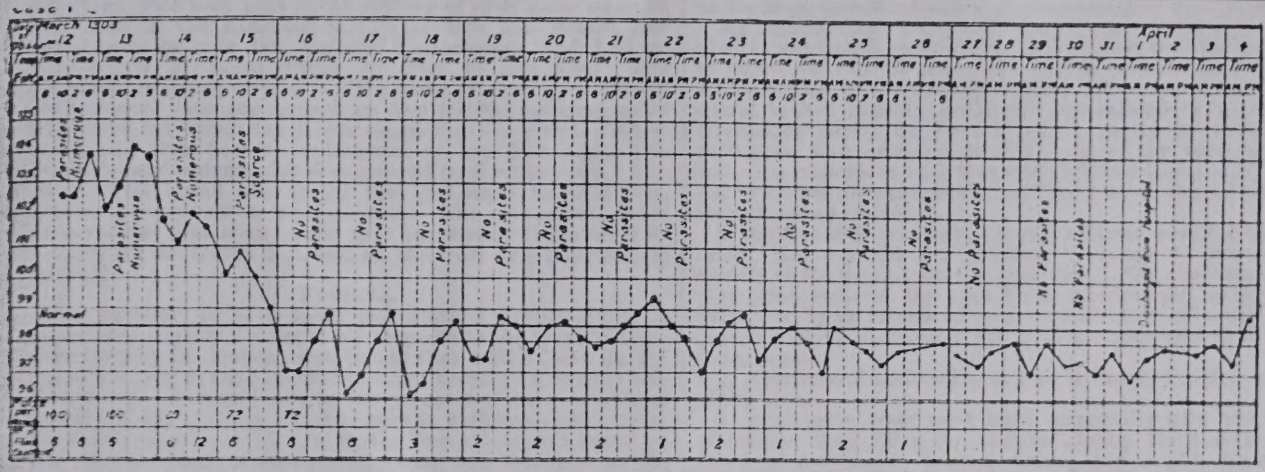


Chart 1. Case

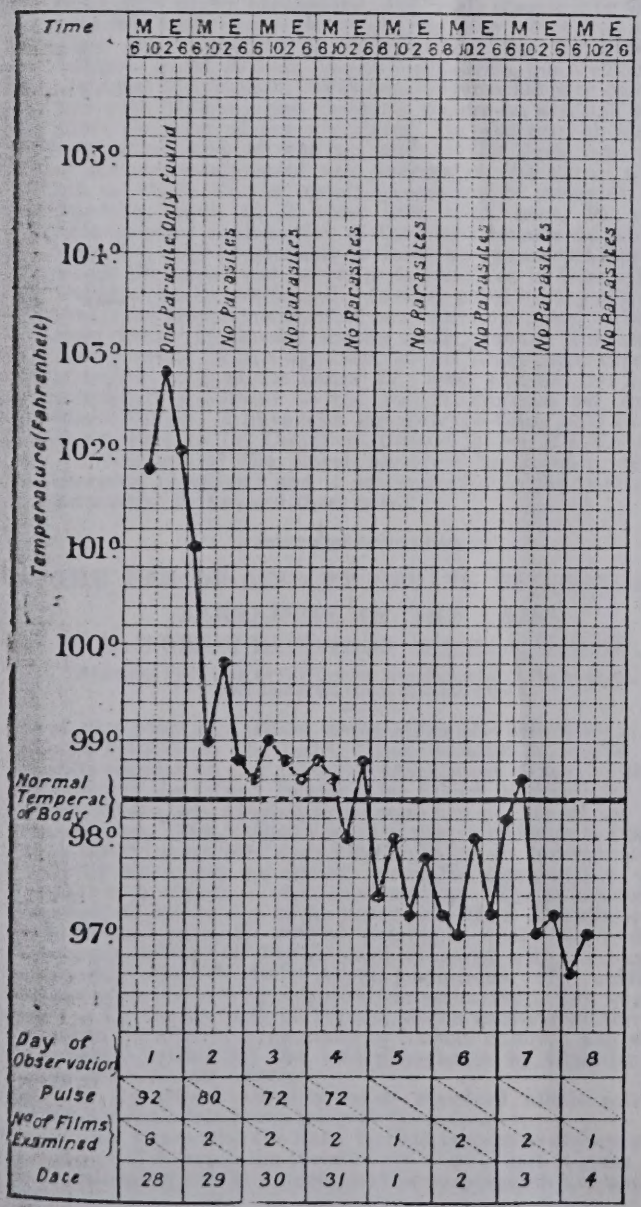


Chart 2.—Case II.

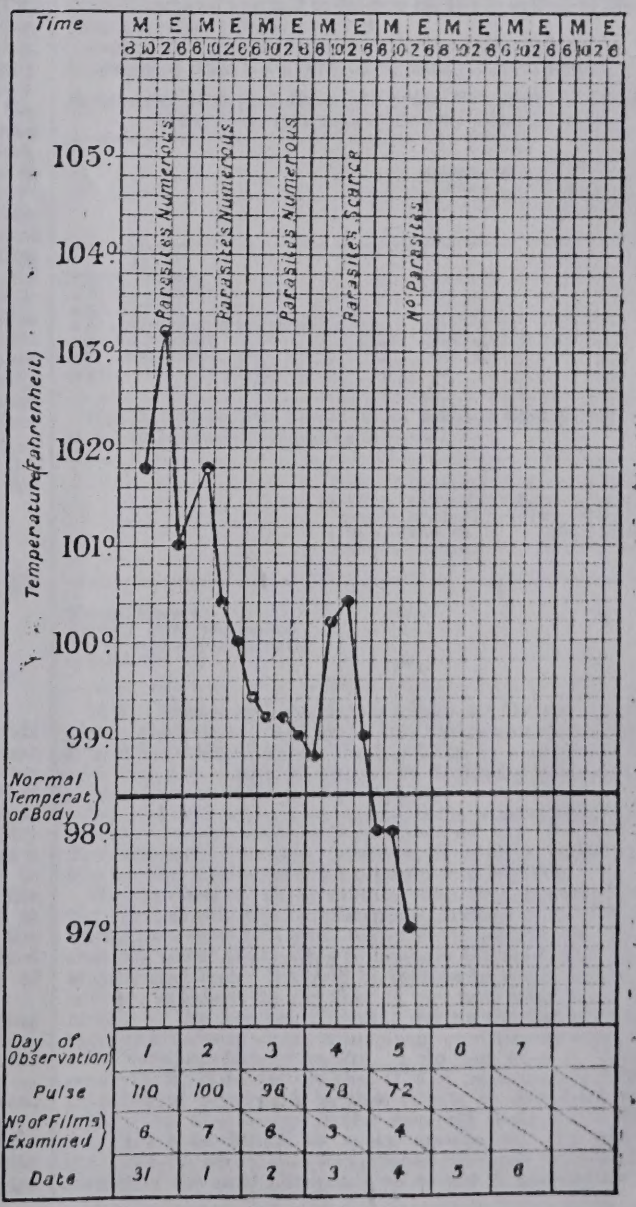
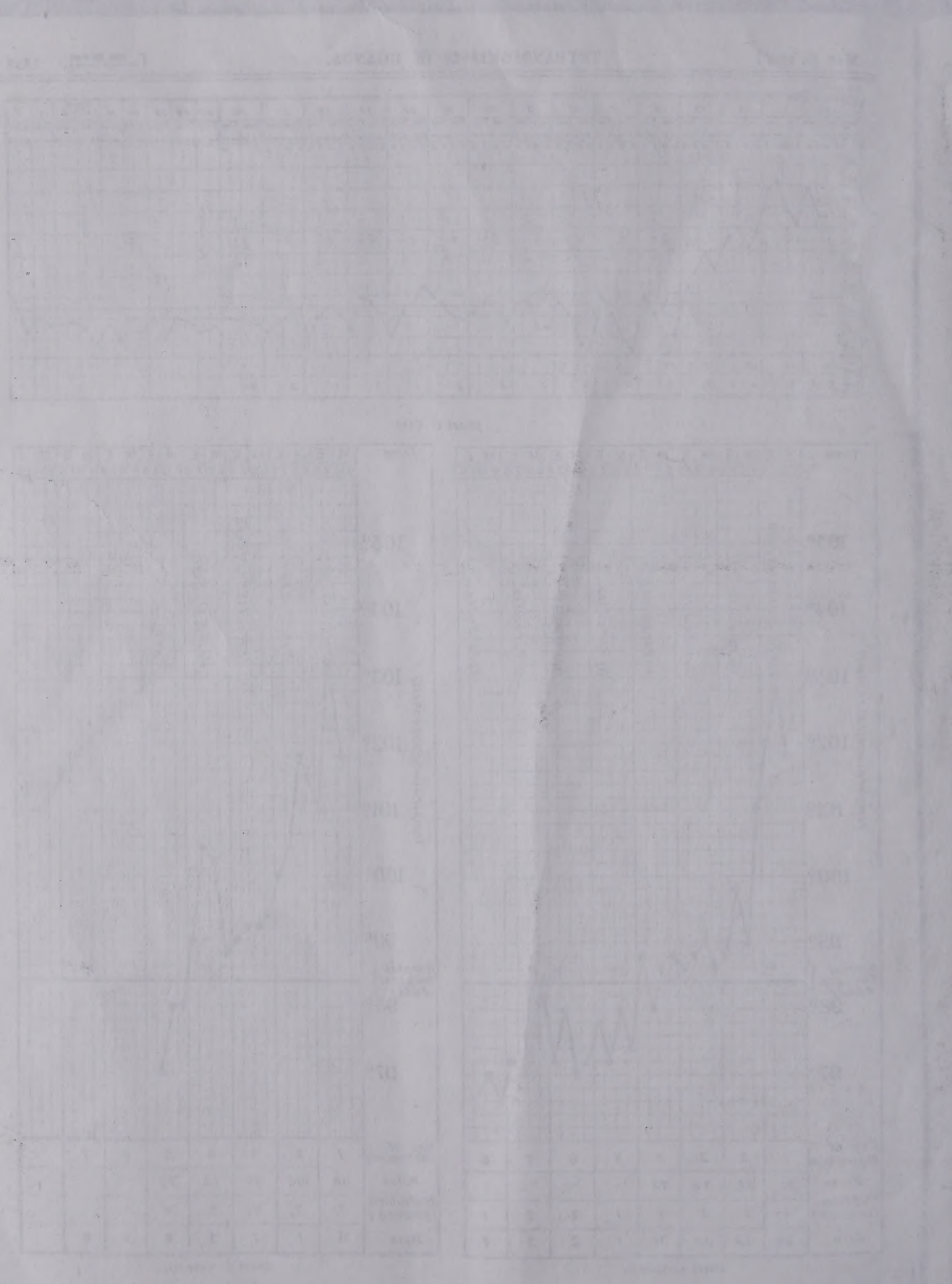


Chart 3. Case III.



quite well up to two days before admission. This patient was a Nubian, who took part in the mutiny of 1898, since when he had been in the Entebbe Gaol. He, like the others, had never been outside the Uganda Protectorate, and had no recollection of being bitten by flies of any sort. His temperature rising to over 103° the same afternoon, gradually sank, almost reaching normal on the fourth morning after admission, on which day it rose again above 100° in the afternoon, and then became subnormal on the fifth day. The headache and oedema also disappeared on the fifth day. The pulse in this, and also in the first two cases, rapid at first, gradually resumed a normal rate. The parasites, more numerous at first than in the first two cases, diminished in number on the fourth day, and on the fifth day disappeared entirely.

REMARKS.

The parasite, in both fresh and stained preparations, is apparently exactly similar in all respects to the trypanosoma described by Dr. Dutton, and also to that which I saw in Dr. Manson's case at the London School of Tropical Medicine last November. Unfortunately undue pressure of other work has prevented my making blood counts in sufficient quantity to be worth recording, though, in the few attempts I made at differential count of leucocytes, there was increase in the percentage of lymphocytes and large mononuclear cells and decrease in the polymorphonuclear cells. I have all these cases still under observation, and shall therefore be able to note any fresh manifestation of symptoms which may occur. They are interesting as showing that the trypanosoma, hitherto found in man only in West Africa, has a wider geographical distribution. They are also remarkable in comparison with Dutton's and Manson's papers on account of the short duration of the symptoms, the absence of hurried respiration, and of wasting, and in the first two cases, of splenic enlargement and oedema of the skin. One is led to think that a certain proportion of cases of short duration, such as I have met with here, in which microscopical examination of the blood reveals no malarial parasites, might reasonably be due to a trypanosoma infection where the number of parasites is small (as in Case II), and therefore easily overlooked. Another point worthy of note is that these cases have occurred in a country reputed to be free from tsetse fly disease among cattle, though the natives have brought me in a fly which Colonel Bruce has assured me is undoubtedly of the tsetse fly group, and he has kindly forwarded specimens to the British Museum for further identification. I have been fortunate in being able to show these cases to Dr. Castellani, Colonel Bruce, R.A.M.C., and Dr. Nabarro, of the Royal Society's Commission for the Sleeping Sickness; and I am indebted to Dr. Moffat for permission to forward these notes.

THE USE OF ACID PHOSPHATE OF SODIUM IN ALKALINITY OF THE URINE.

By ROBERT HUTCHISON, M.D.EDIN., M.R.C.P.,

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A FEW years ago, whilst investigating the behaviour of acids and alkalies in the body, I had occasion to make some experiments on the influence of different drugs on the reaction of the urine. In particular I tried to determine what agents are best adapted to increase the acidity of the renal secretion. The method I adopted was to estimate the acidity of the urine secreted during the night by an individual on a fairly fixed diet on several successive occasions, so as to obtain a standard of normal acidity. The substance the effect of which was to be tested was then administered at bedtime, again on several successive occasions, and the average urinary acidity obtained compared with the standard already observed under normal conditions. The acidity of the urine in these experiments was estimated in two ways:

1. By the method of Freund, which consists in throwing down the alkaline phosphates by barium chloride and subsequently estimating the acid phosphates by titration with uranium nitrate solution.

2. By direct titration with standard alkali solution, phenolphthalein being taken as the indicator.

I am aware that the latter method is open to objection as a means of determining the absolute acidity, but it gives quite trustworthy results for comparative purposes, and, as a matter of fact, I found that it always afforded the same indication as the more accurate method of Freund above described.

My first observations were made with mineral acids—hydrochloric, sulphuric, and phosphoric. I found that the influence of these, even in the largest doses that could be conveniently administered, was extremely slight. The reason for this, no doubt, is that mineral acids are neutralized in the liver or circulation partly by fixed alkalies, partly by ammonium carbonate, and excreted in the form of the corresponding salt. In accordance with this view, I found that the ammonia excretion was always greatly increased after the administration of those substances.

2. Organic acids, of which I tested tartaric, acetic, citric, and lactic, had a slight but distinct tendency to increase the acidity of the urine. On the other hand, the effect was never very great, some of the acid being neutralized as above, as evidenced by an increased excretion of ammonia, and some probably being oxidized in the body and excreted in the form of carbonate.[1]

3. Benzoic and boric acids had no influence on the reaction of the urine.

4. Acid salts were next tried, especially acid phosphate of sodium (NaH_2PO_4), for, that salt being the chief cause of the acid reaction of normal urine, one might reasonably expect its administration to have some effect. This expectation proved to be correct, for sodium acid phosphate had more direct and marked influence on the reaction of the urine than any other substance tried.

Some of the results are shown in the following table, which is compiled from the averages of many observations:

Influence of Medicinal Doses of Various Substances on the Acidity of the Urine (Average of Several Observations).

	Amount of Urine Secreted.	No. of c.cm. of $N_{10}NaOH$ required to Neutralize 10 c.cm. of Urine.
Normal average	240 c.cm.	5·7
½ dr. ac. phosphor dil.	230 ,,	6·6
2 oz., ½ per cent. lactic acid	345 ,,	5·5
2 oz., 2½ per cent. acetic acid	390 ,,	4·1
10 gr. benzoic acid	368 ,,	5·5
45 gr. tartaric acid	270 ,,	6·7
45 gr. sodium acid phosphate	250 ,,	10·0

One may state the result from sodium acid phosphate in terms of Freund's method as follows:

	C.cm. of Uranium Solution required to Precipitate Acid Phosphates in 100 c.cm. Urine.	C.cm. of Uranium Solution required to Precipitate Alkaline Phosphates in 100 c.cm. Urine.
Normal average	46	23
Average after administration of 60 gr. of sodium acid phosphate	92	41

It will be observed that by no means all the acid phosphate given is excreted in that form, but that a considerable proportion is neutralized in the body. This is also shown by the fact that the ammonia output is decidedly raised after the administration of the acid phosphate.

Thus the total ammonia excretion stated in terms of $N_{10}HSO_4$ is: Normal, 148; after 60 gr. sodium acid phosphate, 170.

The ammonia increase, however, is always more marked when either a mineral or an organic acid is given.

Having observed these results, one was encouraged to try the effect of acid sodium phosphate in cases of alkaline urine. This I have done in a great many cases, and the results show that the power of the drug to increase the acidity of the urine is quite manifest. It would be tedious to recite cases, but it will be sufficient to say that it has now been used pretty largely in the London Hospital during the last two years in cases of alkalinity of the urine from cystitis and other causes with very satisfactory results. I do not wish to claim too much for it. I do not say that it will immediately render an ammoniacal urine acid, or that it can be depended upon to bring about that result in the severest cases, but I think it will often be found of great assistance. My colleague Mr. Barnard, has already expressed the high opinion he has formed of the acid phosphate as an aid in keeping the urine

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